

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



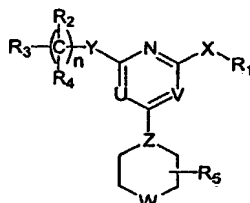
(43) International Publication Date  
6 January 2005 (06.01.2005)

PCT

(10) International Publication Number  
**WO 2005/000404 A2**

- (51) International Patent Classification<sup>7</sup>: **A61P**
- (21) International Application Number: **PCT/US2004/017064**
- (22) International Filing Date: **28 May 2004 (28.05.2004)**
- (25) Filing Language: **English**
- (26) Publication Language: **English**
- (30) Priority Data:  
60/474,550 29 May 2003 (29.05.2003) US  
60/474,502 29 May 2003 (29.05.2003) US  
60/474,410 29 May 2003 (29.05.2003) US
- (71) Applicant (for all designated States except US): **SYNTA PHARMACEUTICALS, CORP.** [US/US]; 45 Hartwell Avenue, Lexington, MA 02421 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **ONO, Mitsunori** [JP/US]; 197 Wood Street, Lexington, MA 02421 (US). **SUN, Lijun** [CN/US]; 148 Depot Road, Harvard, MA 01451 (US). **WADA, Yumiko** [JP/US]; 16 Kings Way #201, Waltham, MA 02451 (US). **KOYA, Kelzo** [JP/US]; 234 Bonad Road, Chestnut Hill, MA 02467 (US). **NAGAI, Masazumi** [JP/US]; 42 Winthrop Road, Lexington, MA 02142 (US).
- (74) Agents: **HSI, Jeffrey, D. et al.**; Edwards & Angell, LLP, P.O. Box 55874, Boston, MA 02205 (US).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— without international search report and to be republished upon receipt of that report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **HETEROCYCLIC COMPOUNDS FOR PREVENTING AND TREATING DISORDERS ASSOCIATED WITH EXCESSIVE BONE LOSS**



(57) Abstract: This invention relates to pyrimidine compounds of formula (I), formula (I') and formula (I''): formula (I) and pharmaceutically acceptable salts, solvates, clathrates, and prodrugs thereof, wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, U, V, W, X, Y, Z, and n are defined herein. This invention also relates to compositions comprising these compounds and methods for using them. The compounds and compositions of this invention are useful to treat or prevent disorders associated with excessive bone loss, including, without limitation periodontal disease, non-malignant bone disorders (such as osteoporosis, Paget's disease of bone, osteogenesis imperfecta, fibrous dysplasia, and primary hyperparathyroidism) estrogen deficiency, inflammatory bone loss, bone malignancy, arthritis, osteopetrosis, and certain cancer-related disorders (such as hypercalcemia of malignancy (HCM), osteolytic bone lesions of multiple myeloma and osteolytic bone metastases of breast cancer and other metastatic cancers).

WO 2005/000404 A2

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
6 January 2005 (06.01.2005)

PCT

(10) International Publication Number  
**WO 2005/000404 A3**

(51) International Patent Classification<sup>7</sup>: **A61K 31/5375**,  
C07D 413/04, 413/14

(21) International Application Number:  
PCT/US2004/017064

(22) International Filing Date: 28 May 2004 (28.05.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/474,550 29 May 2003 (29.05.2003) US  
60/474,502 29 May 2003 (29.05.2003) US  
60/474,410 29 May 2003 (29.05.2003) US

(71) Applicant (for all designated States except US): **SYNTA PHARMACEUTICALS, CORP.** [US/US]; 45 Hartwell Avenue, Lexington, MA 02421 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **ONO, Mitsunori** [JP/US]; 197 Wood Street, Lexington, MA 02421 (US). **SUN, Lijun** [CN/US]; 148 Depot Road, Harvard, MA 01451 (US). **WADA, Yumiko** [JP/US]; 16 Kings Way #201, Waltham, MA 02451 (US). **KOYA, Keizo** [JP/US]; 234 Bonad Road, Chestnut Hill, MA 02467 (US). **NAGAI, Masazumi** [JP/US]; 42 Winthrop Road, Lexington, MA 02142 (US).

(74) Agents: **HSI, Jeffrey, D.** et al.; Edwards & Angell, LLP, P.O. Box 55874, Boston, MA 02205 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

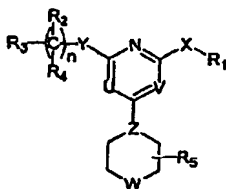
Published:

— with international search report  
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:  
15 September 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **HETEROCYCLIC COMPOUNDS FOR PREVENTING AND TREATING DISORDERS ASSOCIATED WITH EXCESSIVE BONE LOSS**



(I)

(57) Abstract: This invention relates to pyrimidine compounds of formula (I), formula (I') and formula (I''): formula (I) and pharmaceutically acceptable salts, solvates, clathrates, and prodrugs thereof, wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, U, V, W, X, Y, Z, and n are defined herein. This invention also relates to compositions comprising these compounds and methods for using them. The compounds and compositions of this invention are useful to treat or prevent disorders associated with excessive bone loss, including, without limitation periodontal disease, non-malignant bone disorders (such as osteoporosis, Paget's disease of bone, osteogenesis imperfecta, fibrous dysplasia, and primary hyperparathyroidism) estrogen deficiency, inflammatory bone loss, bone malignancy, arthritis, osteopetrosis, and certain cancer-related disorders (such as hypercalcemia of malignancy (HCM), osteolytic bone lesions of multiple myeloma and osteolytic bone metastases of breast cancer and other metastatic cancers).